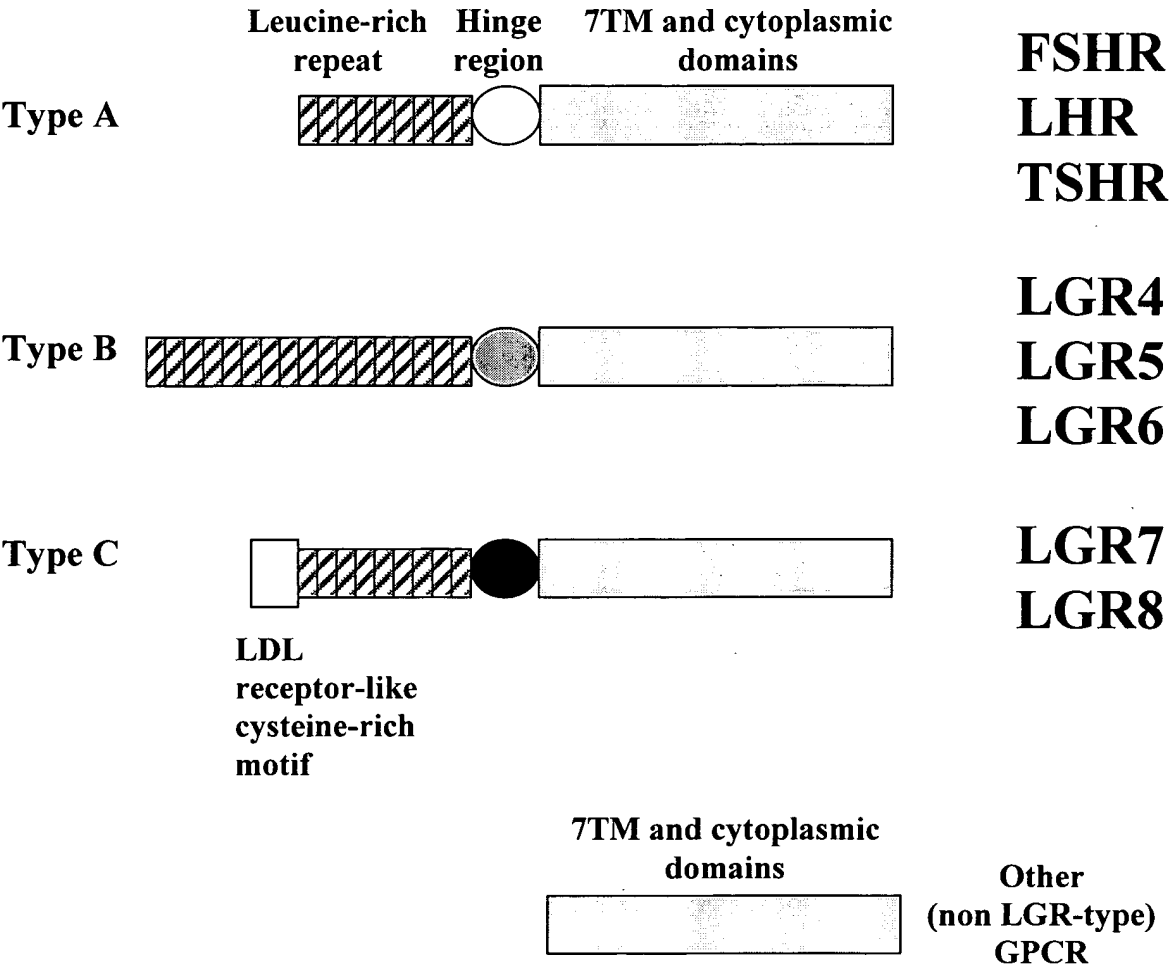




09/647,067
Exhibit 1

Schematic representation of functional domains in LGR family receptors



09/647,067

Exhibit 2

Alignment of LGR7 with LH receptor

Identities = 148/636 (23%), Positives = 289/636 (45%)

```
LGR7 : 89 EAETPECLVGSVPVQCCLCQGLELDCDETNLRAVPSVSSNVTAMSLQWNLIRKLPPDCFKN 148
      EA PE      P C+ G L C      P ++ +T +SL + ++ +P F+
LHR  : 27 EALCPE-----PCNCVPDGA-LRC-----PGPTAGLTRLSLAYLPVKVIPSQAFRG 71

LGR7 : 149 YHDLOKLYL-QNNKITSISIIYAFRGLNSLTKLYLSHNR-ITFLKPGVFEDLHRLEWLIIE 206
      +++ K+ + Q + + I AF L +L+++ + + + + +++PG F +L L++L I
LHR  : 72 LNEVIKIEISQIDSLERIEANAFDNLLNLSEILIQNTKNLRYIEPGAFINLPLGLKLYLSIC 131

LGR7 : 207 DNHLRSRISPPT--FYGLNSLILLVLMNNVLTSLPDKPLCQHMPRLHWLDLEGNHIHNLRN 264
      + + + T F ++ IL + N +T +P      L L GN +++
LHR  : 132 NTGIRKFPDVTKVFSSESFILEICDNLHITIPGNAFQGMNNEVTLKLYGNGFEEVQS 191

LGR7 : 265 LTFISCSNLTVLVMRKN-KINHLNENTFAPLQKLDLDELGLSNKIEENLPPLIFKDLKEL-- 321
      F + + LT L +++N + ++ F      LD+ S K++ LP + ++ L
LHR  : 192 HAF-NGTTLSLELKENVHLEKMHNGAFRGATGPKTLDISSTKLQALPSYGLESIQRLIA 250

LGR7 : 322 -SQLNLSYNPIQKIQANQFD-----YLVKLKSLSLLEGIEISNI----- 358
      S +L P ++ N +      + ++L + S+
LHR  : 251 TSSYSLKKLPSRETFTVNLEATLTYP SHCCAFRNLP TKEQNFSHSISENFSKQCESTVRK 310

LGR7 : 359 --QORMFRPLMNLSHIYFKKFQYCGYAPHVRSCKPNTDGISSLENLLASIIQRVFVWVVS 416
      + ++ ++ S + ++Y P C P D + E+++ RV +W+++
LHR  : 311 VSNKTLYSMLAESELSGWDYEYGFCLPKTPRCAPEPDAPNCPEDIMGYDFLRVLIWLIN 370

LGR7 : 417 AVTCFGNIFVICMRPYIRSENKLYAMSIISLCCADCLMGIYLFVIGGFDLKRGEYNKHA 476
      + GN+ V+ + R + + + +L AD MG+YL +I D + +G+Y HA
LHR  : 371 ILAIMGNMTVLVLLTSRYKLTVPFRFLMCNLSFADFCMGLYLLLIASVDSQTKGQYYNHA 430

LGR7 : 477 QLWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRVPRPGKCR-TITVLILI 535
      W + C G + ++E+SV LT +TLE++ I Y + + R I +++
LHR  : 431 IDWQTGSGCSTAGFFTTFASELSVYTLTVITLERWHTITYAIHLDQKLRLRHAILIMLGG 490

LGR7 : 536 WITGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTESIGAQIYSVAIFLGINLAAFI III 595
      W+ ++A +PL NY + +CFP+ D E+ +Q+Y + I + +N+ AF II
LHR  : 491 WLFSSLIAMLPVVG---VSNYMKVS-ICFPM---DVETLSQVYILTILI-LNVVAFFII 542

LGR7 : 596 VFSYSGSMFYSVHQSAITATEIRNQVKKEMILAKRFFIFVFTDALCWIPIFVVKFLSLLQV 655
      Y ++++V + AT K+ +AK+ ++FTD C PI + +V
LHR  : 543 CACYIKIYFAVRNPELMAT-----NKDTKIAKKMAILIFTDFTCMAPISFFAISAAFKV 596

LGR7 : 656 EIPGTITSWVIFIL--PINSALNPILYTLTRPFK 689
      + T+T+ V+ +L PINS NP LY + T+ F+
LHR  : 597 PLI-TVTNSKVLLVLFYPINSCANPFLYAIFTKTFTQ 631
```

09/647,067

Exhibit 3

Alignment of LGR7 with TSH receptor

LGR7 : 106 LPPDCFKNY-HDLQKLDLQNNKITSISIIYAFRGLNSLTKLYLSHNR-ITFLKPGVFEDLH 163
+P + F+ ++ L L NN TS+ YAF G L +YL+ N+ +T + F ++
TSHR : 167 IPVNAFQGLCNETLTCLKLYNNGFTSVQGYAFNG-TKLDVYLNKNKYLTVIDKDAFGGVY 225

LGR7 : 164 RLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNN-VLTRLDPKPLCQHMPRLHWLDLE-G 221
L+ D + ++ GL L L+ N L +LP H+ R DL
TSHR : 226 SGPSLL--DVSQTSVTALPSKGLEHLKELIARNTWTLKKLPLSLSFLHLTRA---DLSYP 280

LGR7 : 222 NHIHNLRN-----LTFISCSNLTVLVLRKNK-INHLNENTFAPLQKLDLGLSNGKIE 273
+H +N L + C+ ++ +R+ K +N LN +PL + E +LG + +
TSHR : 281 SHCCAFKNQKKIRGILESMLCNESMQSLRQRKSVNALN----SPLHQEYEENLGDSIV- 335

LGR7 : 274 NLPPLIFKDLKELSQLNLSYNPIQKIQANQFDYLVKLKSLSLLEGIEISNIQORMFRPLMN 333
KE S+ ++N A+ + + + + EI Q + P
TSHR : 336 -----GYEKSQFQDTHN-----NAHYVVFEEQED-----EIIGFGQELKNPQEE 376

→ TM1

LGR7 : 334 LSHIYFKKFQY--CGYAPHVRSCKPNTDGISSLENLLASIIQRVFWVVS AVTCFGNIFV 391
+ + Y CG + + C P +D + E+++ R+ VW VS + GN+ FV
TSHR : 377 TLQAFDSHYDYTCGDSEDM-VCTPKSDEFNPCEDIMGYKFLRIVVWFVSLALLGNV FV 435

LGR7 : 392 ICMRPYIRSENKLYAMSIISLCCADCLMGIYLFVIGGFDLKFGEYNKHAQLWMESTHCQ 451
+ + + + +L AD MG+YL +I DL EY HA W C
TSHR : 436 LLILLTSHYKLVNPRFLMCNLAFADFCMGMYLLLIASVDLYTHSEYYNHAIDWQTGP GCN 495

LGR7 : 452 LVGSLAILSTEVSVLLLFTLTLEKYICIVYPRFCVRPGKCR-TITVLILIWITGFIVAFI 510
G + ++E+SV LT +TLE++ I + R R + R +++ W+ F++A +
TSHR : 496 TAGFFT VFASELSVYTLTVITLERWYAITFAMRLDRKIRLRHACAIMVGWVCCFLLALL 555

LGR7 : 511 PLSNKEFFKNYYGTNGVCFPLHSEDTESIGAQIYSVAIFLGINLAAFIIVFSYGS MFYS 570
PL + Y +C P+ DTE+ A Y V + L +N+ AF+I+ + ++ +
TSHR : 556 PLVG----ISSYAKVSICLPM---DTETPLALAYIVFV-LTLNIVAFVIVCCCHVKIYIT 607

LGR7 : 571 VHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPIFVVKFSLQLQVEIPGTITSWV 630
V N K+ +AKR ++FTD +C PI ++L + T+++
TSHR : 608 VRNPQY-----NPGDKDTKIAKRMVLIPTDFICMAPISFYALSAILNKPLI-TVSN SK 660

LGR7 : 631 VIFIL--PINSALNPILYTLTTRPFKE----MIHRFWYNYRQRKSMDSKGQKTYAHHSSG 684
++ +L P+NS NP LY + T+ F+ ++ +F RQ ++ +GQ+ +S+
TSHR : 661 ILLVLFFYPLNSCANPFLYAIFTKAFQRDVFILLSKFGICKRQAQAY--RGQRVPPKNSTD 718

LGR7 : 685 VEM 687
+++
TSHR : 719 IQV 721

09/647,067

Exhibit 4

SEQUENCE ALIGNMENT OF HUMAN LGR7, LGR8, AND TSHR.

LGR8: MIVFLVFKHLFSLRLITMFFLLHFIVLINVKDFALT 36
LGR7: MTSGSVFFYILIFGKYFSHGGG 22

LGR8: 37 QGSMITPSQKGYFPCGNLTKCLERAFHCDKDDCGNGADENCGDTSWATIEGTVHGNANSV----- 100
LGR7: 23 ----QDVKSLGYFPCGNITKCLHQLLHCNIVDDCGNOADEDNCGDNNGWSMQEDKYFASYKMTSQYPF 88

→ LRR1 → LRR2

LGR8: 101 -ALIQEFLKQYEQCCDCKETEIEGVNGDKSVEMISNNVILLSTKKNKTHSEEDKVEIKYTKKKIFLC 169
LGR7: 89 EAETPECLVGSVEVOGLCOGLEIDDETNRRAVSVSSNVVTAMSEOWNLRRKLEPDCEKNMHDLOKLYLC 158
TSHR IEVNAEQGLCNETLTCLK

→ LRR3 → LRR4 → LRR5

LGR8: 170 HNCIRHTSRKAFFGLCNLQILYNHNC-LITLREGIEKDLHOTWLLLDNPITRTSORLETSLNSLFFTS 239
LGR7: 159 NNKITSTISIAERGLNSTTKLYISHNR-LTFYKPGVEEDLHREWLLIEDNHLSTRISPPTEYGLNSIILLV 228
TSHR YNNGFTSVQGYAFNGTK-UDAVYLNKNKYLLVIDKDAFGGVYSGPSLL--DVSQTSVTALPSKGLIEHLKEAIA

→ LRR6 → LRR7 → LRR8

LGR8: 240 MVNNYIEALE-KOMCAQMFQINAVDLEGNRKRYTNSTEILSCDSLTVILFPRNQTGFVPEKTESS-LKN-IG 308
LGR7: 229 LMNNVITRELDKPLCOHMERLHLDOLEGNHNNRNLLLETSCSNLTVLVMRKKNKINHLNENDEAP-LQK-ID 298
TSHR RNTWTLKKLELSLSFLHLTA---DLSYPSCCAFKNQKKIRGILESLMCNESSMQSLRQRKSVNALNSPI

→ LRR9 → LRR10

LGR8: 309 ELDISSNTTETESHLFKDLKLLQKINLSSNMLYHKNOESTKOTOSTDERETEPNTTRMEQPMKN 378
LGR7: 299 ELDIGSNKTEENPELIEKDLKELISQNLNSYNIQKIQANOFTYIVKLKSLSEGLEIENIQOEMERELMN 368
TSHR HQYEENLGDSIV--GYKESKFQDTHNNAHYVFEE---ED-----IIGFGQELKNPQEETLQAF--

→ TM1 → IL1

LGR8: 379 LSHIYKNIERYCSYAPHVRIOMELTDGISSFEDLLANNILRIEIVWMAFIKFCGNLFVIGMRSFTKAENT 448
LGR7: 369 LSHIYENKEQYCGYAPHVRSCKENITDGISSLENLLASITQVFEVWVVSADFCFENIEVCMRPYRSENK 438
TSHR DSH-M--DYTICGDSMD-VGTEKSEDFNPCEIDIMGYKFLRIVVWFVSLALLGNVEVLLILLTSHYKLN

→ TM2 → EL1 → TM3

LGR8: 449 THAMSTKILCCADCLMGVYLFVGIFFDIYRGQYQRYALLWMEVQRMCFEFLAMELSTEVSVLLLTITL 518
LGR7: 439 LYAMSTISLCCADCLMGVYLFVIGGEDERFRGEYNKHAQLWMEVTHQVGSLLAILSTEVSVLLLTITL 508
TSHR PRFLMCNLAFAFDF-C-MGMVILLTASVDLYTHSEYNNHAIDHQTGPGONTAGFFTTFVASELSVYTLTITL

→ IL2 → TM4 → EL2 → TM5

LGR8: 519 EKFLVIVFESNIRPGKROSVILLICIMAGHLIAVIEFWNKDYEGNFYKNGVFPYIYDQEDIGSKG 588
LGR7: 509 EKYICIVYPERCVRPGKCRITVLLILWITGSHVAFIPISNKEFEKNNYGTNGVFPYHSEDTEGIGAI 578
TSHR ERWYAITFAMRDRKIRLRHACAIMVGGVCCCELLALLPLVIG---ISSAKVSICLEM---DTETPLALA

→ IL3 → TM6

LGR8: 589 YSLGIFLGVNLLAFLIVFSYITMECSIQKTALOTTEVRNCFGRVAVANRFEFFIVSDATCWIEVFWK 658
LGR7: 579 YSVATFLGINLAFAEITIVFSYGSMEYSVHQSHTATEIRNOVKKEMILAKREFFIVFTDLGWPIFVVK 648
TSHR MIVFV-LTLNIVAEVIMCCCHVKIYITMRNPQY-----NPGDKDTKIARMAVLIETLFCMAPISFYA

09/647,067

Exhibit 4

→ EL3 → TM7

LGR8: 659 ILSIFRVEEDIMTSWIVLHFLFVNSALNPPLYTLTINFEKDKLKQLHSH-ORKSIFKI--KKSLSTSIV 727

LGR7: 649 FLSLLOVELEGHITSWVVIHLEINSALNPPLYTLTIRPEKEMIHRFWYNYRORKSMSDK--GOKTYAPFI 718

TSHR LSAILLNKPLITVSNKILLVLE-YELNSCANEFLYAIFTKAFQRDVFILISFGICKRQAQAYRCORVPPKNST

LGR8: 729 WIDSSSLKLGVLNKITLGDSIMKPVS* 755

LGR7: 719 WVEIMWPLQEMPPELMKPDLEFTYPEMSLISQSTRLNSYS* 757

TSHR DIQV



RECEIVED
OCT 29 2003
TECH CENTER 1600/2900

5/8

>Alignment of LGR7-L with LGR7-S

Query=LGR7-L

Sbjct=LGR7-S

```
Query: 1  MTSGSVFFYILIFGKYFSHGGGQDVKCSLGYFPCGNITKCLPQLLHCNGVDDCGNQADE 60
          MTSGSVFFYILIFGKYFSHGGGQDVKCSLGYFPCGNITKCLPQLLHCNGVDDCGNQADE
Sbjct: 1  MTSGSVFFYILIFGKYFSHGGGQDVKCSLGYFPCGNITKCLPQLLHCNGVDDCGNQADE 60

Query: 61  NCGDNNGWSMQFDKYFASYKMTSQYPFEAETPECLVGSVPVQCLCQ---GLELDCDETN 117
          NC                               V V C C   GLELD +
Sbjct: 61  NC-----VVVLCQCMSLPGLELDWMKP- 82

Query: 118  LRAVPSVSSNVTAMSLQWNLIRKLPDCFKNYHDLQKLYLQNNKITSISIIYAFRGLNSLT 177
          +VPSVSSNVTAMSLQWNLIRKLPDCFKNYHDLQKL LQNNKITSISIIYAFRGLNSLT
Sbjct: 83  FTSVPSVSSNVTAMSLQWNLIRKLPDCFKNYHDLQKLDLQNNKITSISIIYAFRGLNSLT 142

Query: 178  KLYLSHNRIITFLKPGVFEDLHRLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNNVLTRL 237
          KLYLSHNRIITFLKPGVFEDLHRLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNNVLTRL
Sbjct: 143 KLYLSHNRIITFLKPGVFEDLHRLEWLIIEDNHLSRISPPTFYGLNSLILLVLMNNVLTRL 202

Query: 238  PDKPLCQHMPRLHWDLEGNHIHNLRLNLTIFISCSNLTVLVMRKKNKINHLNENTFAPLQKL 297
          PDKPLCQHMPRLHWDLEGNHIHNLRLNLTIFISCSNLTVLVMRKKNKINHLNENTFAPLQKL
Sbjct: 203 PDKPLCQHMPRLHWDLEGNHIHNLRLNLTIFISCSNLTVLVMRKKNKINHLNENTFAPLQKL 262

Query: 298  DELDLGSNKIENLPPLIFKDLKELSQLNLSYNPIQKIQANQFDYLVKLKSLSLLEGIEISN 357
          DELDLGSNKIENLPPLIFKDLKELSQLNLSYNPIQKIQANQFDYLVKLKSLSLLEGIEISN
Sbjct: 263 DELDLGSNKIENLPPLIFKDLKELSQLNLSYNPIQKIQANQFDYLVKLKSLSLLEGIEISN 322

Query: 358  IQQRMFRPLMNLSHIYFKKFQYCGYAPHVRSCKPNTDGISSLENLLASIIQRFVFWVWSA 417
          IQQRMFRPLMNLSHIYFKKFQYCGYAPHVRSCKPNTDGISSLENLLASIIQRFVFWVWSA
Sbjct: 323 IQQRMFRPLMNLSHIYFKKFQYCGYAPHVRSCKPNTDGISSLENLLASIIQRFVFWVWSA 382

Query: 418  VTCFGNIFVICMRPYIRSENKLYAMSIIISLCCADCLMGIYLFVIGGFDLKFRGEYNKHAQ 477
          VTCFGNIFVICMRPYIRSENKLYAMSIIISLCCADCLMGIYLFVIGGFDLKFRGEYNKHAQ
Sbjct: 383 VTCFGNIFVICMRPYIRSENKLYAMSIIISLCCADCLMGIYLFVIGGFDLKFRGEYNKHAQ 442

Query: 478  LWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRCVPRPGKCRITITVLILIWI 537
          LWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRCVPRPGKCRITITVLILIWI
Sbjct: 443 LWMESTHCQLVGSLAILSTEVSLLLLTFLTLEKYICIVYPFRCVPRPGKCRITITVLILIWI 502

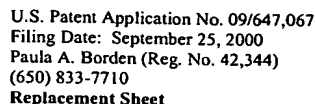
Query: 538  TGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTE SIGAQIYSVAIFLGINLAAFIIVF 597
          TGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTE SIGAQIYSVAIFLGINLAAFIIVF
Sbjct: 503 TGFIVAFIPLSNKEFFKNYYGTNGVCFPLHSEDTE SIGAQIYSVAIFLGINLAAFIIVF 562

Query: 598  SYGSMFYSVHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPFVVKFLSLLQVEI 657
          SYGSMFYSVHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPFVVKFLSLLQVEI
Sbjct: 563 SYGSMFYSVHQSAITATEIRNQVKKEMILAKRFFFIVFTDALCWIPFVVKFLSLLQVEI 622

Query: 658  PGTITSWVVIFILPINSALNPILYTLTTRPFKEMIHRFWYNYRQRKSMDSKGQKTYAPSF 717
          PGTITSWVVIFILPINSALNPILYTLTTRPFKEMIHRFWYNYRQRKSMDSKGQKTYAPSF
Sbjct: 623 PGTITSWVVIFILPINSALNPILYTLTTRPFKEMIHRFWYNYRQRKSMDSKGQKTYAPSF 682

Query: 718  IWVEMWPLQEMPPPELMKPDLTYPCEMSLISQSTRLNSYS 757 (SEQ ID NO:06)
          IWVEMWPLQEMPPPELMKPDLTYPCEMSLISQSTRLNSYS (SEQ ID NO:09)
Sbjct: 683 IWVEMWPLQEMPPPELMKPDLTYPCEMSLISQSTRLNSYS 722 (SEQ ID NO:08)
```

FIG. 5



OCT 29 2003

TECH CENTER 1600/2900

6/8

Signal peptide

LGR4 MPGPLGLLLCFLALGLLGSAGPSGA (SEQ ID NO:10)
LGR5 MDT SRLGVLLSLPVLQLATG (SEQ ID NO:11)
LHR MKQRFSAQLLLKLLLLQPPLPRA (SEQ ID NO:12)
FSHR MALLLVSLAFLSLGSG (SEQ ID NO:13)
TSHR MRPADLLQLVLLLDLPDLGG (SEQ ID NO:14)

N-flank cysteine-rich sequence

```

LGR4      APPL AA-P S DGDR---RVD SGKGLTAVPEGLSAFTQA (SEQ ID NO:15)
LGR5      GSSPRSGVLLRG P-TH H EPDGRMLLRVD SDLGLSELPSNLSVFTSY (SEQ ID NO:16)
LHR       LREAL P-EP N VPDG--ALR-- PGPTAGLTR (SEQ ID NO:17)
FSHR      HHRI H SNRVFL---- QESKVTEIPSDLFRNAIE (SEQ ID NO:18)
TSHR      MG SPPP E HQEED--FRVT KDIIQRIPLPPSTQT (SEQ ID NO:19)

```

Leucine-rich repeats

LGR4	DISMNNITQLPED	KSFPFLEELQLAGN	--	SL	HPKALSG	KE	KVLTQ	--	Q
LGR5	DLSMNNISQLLPNPLPSLHFLLEELRLAGNA	--	TY	PKGA	TG	YS	KVLMQ	--	Q
LHR	SLAYLPVKVIPSQ	RLNVEVIKIEISQI	S-	ER	EANA	DN	LN	SEIIQ	TK
FSHR	RFVLTKLRLVIQKG	SGFGDLKIEIISON	V-	EV	EADV	SN	PK	HEIRIEKAN	-
TSHR	KLIETHLRLTIPSH	SNLPNISRIYVSI	-VT	QQLES	SHS	YN	SKVTHIEIR	TR	-

LGR4	RTV-	SE	IHG	SA	QS	RLDA	H-	TSV	EDS--	FEGVLQLRH	WLD	S-L-	EV	VR
LGR5	RHV-	TE	LQN	RS	QS	RLDA	H-	SYV	P-SC-	FSGLHSLRH	WLD	A-L-	E	VQ
LHR	RYIE	-G	FIN	PG	KY	SIC-	TG	RKF	DVTKVFSSES	SNFI	-EIC	LHI-	T	GN
FSHR	LYIN	-E	FQN	PN	QY	LIS-	TG	KHL	DVHK-	IHSLOKVL-	DIQ	INIH	-	ERN
TSHR	TYID	-D	LKE	PL	KF	GIF-	TGLKMF	DLTK	-VYSTD	DIFFI	EIT	PYM-	S	VN

LGR4	PLSN	P-TLQA	T	AL	NISSIPDF	T	LSS	VV	H	HN	K-IKSLSQHC	D	LDN-LE	
LGR5	A	RS	S-ALQAMT	AL	KIHHPDY	G	LSSVVV	H	HN	R-IHSLGKCC	D	LHS-LE		
LHR	A	QGMNNE	SVT	K	YG	GFEVQSH	-	GTT	TS	E	KE	VHLEKMHGA	R	A-TGPK
FSHR	S	VG	SFESVI	W	NK	GQIEIHC	-	GTTQ	DE	N	SD	NNLEELPNDV	H	A-SGPV
TSHR	A	QG	CNETLT	K	YN	GFTSVQGY	-	GTK	DAVY	NK	KYLTVIDKDA	G	VYSGPS	

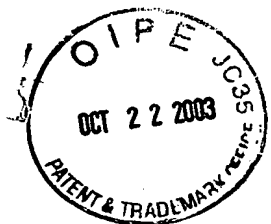
```

LGR4  T  LNYNYLDEF Q-AIKA PS KELGFHSNSISVI D-GA GGNPL RTIH - DNPLS
LGR5  T  LNYNNLDEF T-AIRT SN KELGFHSNNIRSI E-KA VGNP S ITIHF- DNPIQ
LHR   T  ISSTKLQAL SYGLESIQ R I-ATS-SYSLKKL SRET V-N-- LEAT T -----(SEQ ID NO:22)
FSHR  I  ISRTRHSL SYGLEN KK R-ARSTYN-LKKL TLEKLVA--- MEAS T -----(SEQ ID NO:23)
TSHR  L  VSOTSVAL SKGLEH KE I-ARNTWT-LKKL LSL S LH--- TRAD S -----(SEQ ID NO:24)

```

LGR4 FVGNSAFHNLSDLHCLVIRGASLVQWFPNLTGTVHLESILTLTGTKISSIPDDLQCNQKML
LGR5 FVGRSAFQHLPELRTLTLNGASQITEFPDLTG TANLESILTLGAQISSLPQTVCNQLPNL
LHR -----
FSHR -----
TSHR -----

FIG. 6A



RECEIVED
OCT 29 2003
TECH CENTER 1600/2900

7/8

RTLDLSYNNIRDLPSPNGCRALEEISLQNRQISLIKENTFQGLTSRILDLSRNLIREIH
QVLDLSYNLLEDLPSPSVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRSLNLAWNKAIIH

SGAFAKLGTITNLDVSFNETSFPTTEGLNGLNQLK (SEQ ID NO:20)
PNAFSTLPSLIKLDLSSNLLSSFPITGLHGLTHLK (SEQ ID NO:21)

C-flank cysteine-rich sequence

LGR4	LVGNFKLKDALAARDFANLRSLSV YAYQ	WGCDSLCKLNTEDNSPQEHSVTKEGA
LGR5	LTGNHALQSLISSENFPELVKVIEM YAYQ	GVCENAYKISNQWNKGDNSMDDLHKK
LHR	----- --SH	RNLPTKEQNFSSHSISENFSKQCESTVR
FSHR	----- --SH	ANWRRQISELHPICNKSILRQEVDMYT
TSHR	----- --SH	KNQKKIRGILESMLCNESMQLSRQRK

LGR4	TDAANVTSTAENE HS-----	
LGR5	DAGMFQAQDERDL DF-----	
LHR	KVSNKTYSSMLA SE-----	
FSHR	QTRGQRSSLAEDN SS-----	
TSHR	SVNALNSPLHQEY ENLGDSIVGYKEKSKFQDTHNNAHYVVFEEQEDEIIGFGQELKNP	

LGR4	-----QIIH T STGA K	YLLGSWMI (SEQ ID NO:25)
LGR5	-----LLDFEEDLKALHSVQ S SPGP K	HLLDGWLI (SEQ ID NO:26)
LHR	-----LSGWDYEGFCLPKTPR- A EPDA N	DIMGYDFL (SEQ ID NO:27)
FSHR	YSRGFDMTYTEFDYDLCEVVDVT S KPDA N	DIMGYNIL (SEQ ID NO:28)
TSHR	QEETLQAFDSDHYDTICGDSSEDMV T KSDE N	DIMGYKFL (SEQ ID NO:29)

Transmembrane

	TM 1	TM 2
LGR4	LTV F FLV LLF LL ILTVFA CSS PASKLFIGLISVSNLLM IYTGILTFL AVSW	
LGR5	IGV T AV LTC AL TSTVFR PLYISPIKL IGVIAAVNMLT VSSAVL G AF F	
LHR	VLI L NI IMG MT LFLVLT RYK TVPRF MCNLSFADFCM LYLLLI S SQ K	
FSHR	VLI F SI ITG II LVILTT QYK TVPRF MCNLAFADLCI IYLLLI S IH K	
TSHR	IVV FVSL LLG VF LLILLT HYK NVPRF MCNLAFADFCM MYLLLI S LY H	

	TM 3
LGR4	GRFAEFG W E S KV SLA S SA FL LAAV SVFAKDLMKHKGKSSH QF
LGR5	GSFARHGAW EN V HVI LSI S FL LAA GFSVKYSARFET APFSSL
LHR	GQYYNHA D Q S ST FT L YT VIT WHTITYAIHLDO LR HA
FSHR	SQYHNHA D Q A DA FT L YT AIT WHTITHAMQLDC VQ HA
TSHR	SEYYNHA D Q P NT FT L YT VIT WYAITFAMRLDR IR HA

FIG. 6B



RECEIVED
OCT 29 2003
TECH CENTER 1600/2900

TM 4					TM 5				
LGR4	QVAALLALLGAAVAGCF	FHGGQ	SASPL	FPTGETPSLGFTVTLVL	SL	LLMA			
LGR5	KVIILLCALLALTM AV	L G K	GASPL	LPFGEPSTMG MVALIL	SLC	LMMT			
LHR	ILIMLGGLFSSLI ML	V V N	MKVSIF	MDVETTLSSQV ILTILI	VV	FIIC			
FSHR	ASVMVMGWIFAFAA LF	IF I S	MKVSIF	MDIDSPLSQL VMSLLV	VL	VVIC			
TSHR	CAIMVGWVCCFLL LL	V I S	AKVSI	MDTETPLALA IVFVLT	IV	VIVC			
TM 6									
LGR4	II T L	CNL-EKEDLSENSQSSVI	HV W	NCIFFC	VA	FSFAPLITAIS	SPEI		
LGR5	IA T L	CNL-DKGDLENIW CSMV	HI L L	NCILNC	VA	LSF SLINLTF	SPEV		
LHR	AC I I	FAVRNPELMATNK TKIA	KM I	DFTCMA	IS	FAI AAFKVPL	TVTN		
FSHR	GC IHI	LTVRNPNISSSS TRIA	RM M	DFLCMA	IS	FAI ASLKVPL	TVSK		
TSHR	CCHV I	ITVRNPQYNPGDK TKIA	RM V	DFICMA	IS	YAL AILNKPL	TVSN		
TM 7									
LGR4	M SVTLI	F LPA L	V VF N	(SEQ ID NO:30)					
LGR5	I FI LVVV	LPA L L	IL N	(SEQ ID NO:31)					
LHR	S VL VL	Y INS A	F AI T	(SEQ ID NO:32)					
FSHR	A IL VL	H INS A	F AI T	(SEQ ID NO:33)					
TSHR	S IL VL	Y LNS A	F AI T	(SEQ ID NO:34)					
C-terminal tail									
LGR4	PK KE	WKL KRRVTRKHGSVSVS	ISSQGGCGEQDFYYDCGMYSHLQGNLTVCDCCESFL						
LGR5	PH KE	LVS RKQTYVWTRSKHPSLMS	INSDDVEKQSCDSTQALVTFTSSSITYDLPPSS						
LHR	KT QR	FFL LSKFGCCKRRAELYRRKDF	SAYTSNCKNGFTGSNKPSQSTLKLSTLHCQG						
FSHR	KN RR	FFI LSKCGCYEMQAQIYRTETS	STVHNTHPRNGHCSSAPRVTVNGSTYILVPLS						
TSHR	KA QR	VFI LSKFGICKRQAQAYRGQR	VPPKNSTDIQVQKVTHDMRQGLHNMEDVYELI						
LGR4	LTKPVSC	KHLIKSHS	CPVLTAASCORPEAYWSDCGTQSAHSDYADEEDSFVSDSSDQVQA						
LGR5	VPSPAYF	VTESCHLSSVAFVPCL	(SEQ ID NO:36)						
LHR	TALLDK	TRYTEC	(SEQ ID NO:37)						
FSHR	HLAQN	(SEQ ID NO:38)							
TSHR	ENSHLTP	KKQGQISEEYMQTVL	(SEQ ID NO:39)						
LGR4	CGRACFY	QSRGFPLVRYAYNLQVRVD	(SEQ ID NO:35)						

FIG. 6C